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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/305,084	05/04/1999	Robert J. Schneider	5914-080-999	1583

20582 7590 02/25/2003

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EXAMINER

HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 02/25/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/305,084

Applicant(s)

SCHNEIDER ET AL.

Examiner

Alana M. Harris, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 14-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 14-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Claims 1-5 and 14-20 are pending.

Claim 4 has been amended.

Claims 16-20 have been added.

Claims 1-5 and 14-20 examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. The rejection of claims 1-5, 14, 15 and newly added claims 16-20 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained and made.

Applicants argue that “[t]he Examiner appears to be positing a rule that an Applicant must be limited to claiming only what is present in the working examples...”. “Applicants submit that the specification does adequately describe the entire scope of genus of compounds to be used in the claimed methods of the invention” and “the specification has provided a description of unifying characteristics that distinguish the members of the genus of compounds to be used in the methods of the invention, i.e., the ability to selectively antagonize ETB.” Furthermore, Applicants aver that “[o]ne of skill in the art can easily subject candidate compounds to *in vitro* assays to discern genus members from non-genus members” and “...*any* compound can be determined by one...to be either inside or outside of the genus without resorting to undue experimentation.” Applicants’ arguments filed December 4, 2002 have been fully considered but they are not persuasive.

Applicants’ claims continue to embrace not only peptides, such as BQ788 but RNAs, small molecule inhibitors, antisense molecules and ribozymes, see page 25, lines 12-19. And while it is true that Applicants need not present or disclose every species in a genus they must present a representative number of species when the claims broadly encompass a vast and diverse genus.

Furthermore, Applicants directed arguments to 112, 1st enablement issues, such as undue experimentation, which were not of record. Applicants assert that there are *in vitro* assays capable of discerning whether or not candidate compounds are within or outside of the genus and this type of experimentation would not be undue burden. Assuming that the 112, 1st rejection was such it is of record that “[v]ery few selective

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ETB antagonists have been identified.”, see page 10, line 23. Seemingly, the state of the prior art is such that selective ETB antagonists are not easily identified and that there are numbers of yet to be discovered molecules that could be deemed selective ETB antagonists. Accordingly, as set forth in the previous office action Applicants are not entitled, nor is the specification enabled for the use of all ETB antagonists capable of playing a role in preventing the downregulation of E-cadherin in a cancer cell or in the cascade leading to the early developments associated with melanoma development. Applicants are not permitted to claim all selective ETB antagonists and mimics thereof that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue.

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Claim Rejections - 35 USC § 102

5. The rejection of claims 1-4 and 14-18 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 6,063,911 (filed December 22, 1998) is maintained and made.

Applicants argue that patent '611 does not describe the claimed method and that the disclosed compound, RO61 is a non-specific, non-peptide inhibitor of both endothelin receptors. This argument has been found unpersuasive.

The anticipatory patent discloses the claimed method. In view of the absence of a definition of selective antagonists of endothelin B receptor and the examination of the within reasonable breadth, RO61 cannot be excluded as a selective antagonist to an endothelin B receptor. Moreover, the claims are not written wherein the antagonist is exclusive for the endothelin B receptor. Because the disclosed compound definitely binds the receptor it is regarded as selective and meets the limitations of the claims. Additionally, the disclosed compound effective in the disclosed method of treating cancer inherently would prevent (a) the downregulation of E-cadherin in the cancer cell; (b) the downregulation of β -catenin in the cancer cell; (c) the downregulation of p120^{CTN}; and (4) the increased activity of caspase 8 in the cancer cell.

6. The rejection of claims 1, 4 and 14-18 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,382,569 (January 17, 1995/ Reference AP on IDS) is maintained and made.

Applicants arguments are of record in Exhibit 2, submitted December 4, 2002 and Paper number 10, received August 23, 2001. As set forth in the previous paragraph the claims are not written wherein the antagonist is exclusive for the endothelin B receptor. Because the disclosed compounds definitely bind the receptor they are regarded as selective and meet the limitations of the claims. Additionally, the disclosed compounds effective in the disclosed method of treating cancer inherently would prevent (a) the downregulation of E-cadherin in the cancer cell; (b) the downregulation

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of β -catentin in the cancer cell; (c) the downregulation of p120^{CTN}; and (4) the increased activity of caspase 8 in the cancer cell.

Conclusion

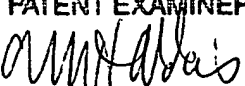
7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Lahav et al. An endothelin receptor B antagonist inhibits growth and induces cell death in human melanoma cells in vitro and in vivo (Proc. Natl. Acad. Sci, USA 96:11496-1150, September 1999).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA HARRIS
PATENT EXAMINER


Alana M. Harris, Ph.D.
February 24, 2003